REMARKS

Summary of the Invention and the Argument

The present invention recites methods for treating nicotine addiction and aiding smoking cessation in a human by administering a therapeutically effective amount of (-)-bupropion, or a pharmaceutically acceptable salt thereof, that is substantially free of its (+)-stereoisomer. As defined in the specification, "substantially free of (+)-stereoisomer," in the context of the present invention, means that the composition contains a greater proportion of the (-)-isomer of bupropion than the (+)-isomer with a clearly defined range of the isomers' relevant amounts.

Therefore, the definition provided in the present invention for (-)-bupropion clearly defines and distinguishes it from racemic bupropion, which contains equal amounts of (-)-bupropion and (+)-bupropion. Furthermore, the specification provides examples and preferred embodiments of the recited (-)-bupropion. Applicants submit that the claim language of the present application is definitive under the requirements of 35 U.S.C. § 112, Second Paragraph, and that one of ordinary skill in the art, based on the definition and other disclosures made in the present invention, would clearly understand what is claimed.

Applicants further submit that the cited reference by Coutts, whether alone or in combination with the alleged admission by Applicants, fails to suggest the presently claimed invention. The specification of the current application discloses that racemic mixture of bupropion is commercially available for the treatment of depression and achieve smoking cessation. There is no suggestion in the prior art, nor any admission by Applicants, regarding the use of the (-)-stereoisomer of bupropion as presently claimed. Coutts, on the other hand, contains no disclosure regarding the use of (-) bupropion. All Coutts discloses is that different enantiomers of a compound may possibly possess different pharmodynamic properties. Regarding bupropion, Coutts merely discloses that racemic bupropion is a drug that possesses one chiral center and is used as an antidepressant. Moreover, Coutts does not disclose or suggest that enantiomers of bupropion have different pharmacological properties, much less that (-) bupropion is pharmacologically preferable over its (+) counterpart.

Therefore, Coutts, alone or in combination with the disclosure in Applicants' specification, fails to disclose or suggest that (-) bupropion can be preferentially used to treat smoking addiction over its (+) counterpart, as presently claimed.

Rejection Under 35 U.S.C. § 112, Second Paragraph, Should be Withdrawn

Claims 16, 18-22, 25-29, 43, 45-49, 52-55, and 79-80 have been rejected by the Examiner under 35 U.S.C. §112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter for the reasons set forth on page 2 of the Office Action. More specifically, the Examiner alleges that it is not clear how much (+)-stereoisomer the recitation "substantially free of its (+) isomer" is intended to exclude. Applicants respectfully traverse this rejection.

As submitted by Applicants in the previous response to Office Action dated May 16, 2001, the term "substantially free of" is fully and clearly defined in the specification of the current application. As seen at page 13, line 27 to page 14, line 12 of the specification, the term "substantially free of" was given a clear meaning by Applicants, and specific examples and preferred embodiments were also disclosed. Therefore, Applicants respectfully submit that the term "substantially free of" would be readily understandable to persons with ordinary skills in the art.

In addition, the words of a claim are given their ordinary meaning, unless it appears that the inventor used them differently. *See, e.g., Hoganas AB v. Dresser Industries, Inc.* 9 F.3d 948, 951 (Fed. Cir. 1993). The ordinary meaning of the word "substantial" does not impose limitations as to the minimum percentage or amount of the objects that the word modifies. As for the question posed by the Examiner in the current Office Action that whether the intent is that the amount of (-) bupropion to (+) bupropion can be 51% to 49%, Applicants respectfully submit that such interpretation is possible within the broadest construction of Applicants' definition. However, it would be obvious to one of ordinary skill in the art that obtaining a ratio of 51 to 49 in literal sense is improbable for practical considerations. Therefore, Applicants provided examples and preferred embodiments of "substantially free of" in the specification.

Furthermore, Applicants respectfully point out that even if the ratio of 51 to 49 can be obtained, the fact that the ratio may be 51 to 49 does not render the term "substantially free of" indefinite. As the Examiner is well aware, "a patentee can be his own lexicographer provided the patentee's definition, to the extent it differs from the conventional definition, is clearly set forth in the specification." *See Beachcombers, International, Inc. v. Wilde Wood Creative Products, Inc.*, 31 F.3d 1154, 1158 (Fed. Cir. 1994). Here, the definition given by Applicants does not differ from the conventional definition of the term. But assuming, *arguendo*, encompassing the ratio of 51 and 49 by the term renders it somehow different from the conventional meaning, the definition provided in the specification is sufficiently clear such that one of ordinary skill in the art can readily understand.

For the foregoing reasons, Applicants respectfully submit that the term "substantially free of" is sufficiently clear as not to be indefinite, and thus the rejection under 35 U.S.C. § 112, second paragraph, should be withdrawn.

Rejection Under 35 U.S.C. § 103(a) Should Be Withdrawn

Claims 16, 18-22, 25-29, 43, 45-49, 52-55, and 79-80[1] are rejected under 35 U.S.C. § 103(a) as being unpatentable over Applicant's alleged admission that the method of using bupropion to treat smoking addiction and aid in smoking cessation is known, in view of Coutts *et al.*, *Chirality* 1:99-120 (1989) ("Coutts"). Applicants respectfully traverse this rejection.

Applicants wish to once again invite the Examiner's attention to the three basic criteria that must be met to establish a case of *prima facie* obviousness. First, there must have been, at the time of the invention, a motivation to combine the references cited. Second, the alleged prior art must teach or suggest all of the limitations of the claims alleged to be obvious. Third, there must have been, at the time of the invention, a reasonable expectation of success. *MPEP* § 2142. In contrast, an invitation to experiment or a

[1] The rejection is directed to claims 16-29 and 43-55 in the Office Action. Since the amendments in the previous Response to Office Action were made into record, Applicants assumed that this rejection is directed to all currently pending claims.

contention that an invention is "obvious to try" does not render claims *prima facie* obvious, *see, e.g., Gillette Co. v. S. C. Johnson & Sons, Inc.*, 919 F.2d 720, 725 (Fed. Cir. 1990); *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988); *Jones v. Hardy,* 727 F.2d 1524, 1530; *Hybritech, Inc. v. Monoclonal Antibodies, Inc.,* 802 F.2d 1367, 1380 (Fed. Cir 1986) *cert. denied*, 480 U.S. 947 (1987) (prior art references were an invitation to try but did not show obviousness because they did not suggest how to accomplish the goal).

The specification of the current application discloses that racemic mixture of bupropion is commercially available for the treatment of depression and achieve smoking cessation. *See, e.g.*, specification at page 2, lines 3-13. There is no suggestion in the prior art, nor any admission by Applicants, regarding the use of the (-)-stereoisomer of bupropion as presently claimed. Coutts, on the other hand, contains no disclosure regarding the use of (-) bupropion. All Coutts discloses is that different enantiomers of a compound may possibly possess different pharmodynamic properties. Regarding bupropion, Coutts merely discloses that racemic bupropion is a drug that possesses one chiral center and is used as an antidepressant. *See Coutts* at page 113, cols. 1-2. Moreover, Coutts does not disclose or suggest that enantiomers of bupropion have different pharmacological properties, much less that (-) bupropion is pharmacologically preferable over its (+) counterpart. Therefore, Coutts, alone or in combination with the disclosure in Applicants' specification, fails to disclose or suggest that (-) bupropion can be preferentially used to treat smoking addiction over its (+) counterpart, as presently claimed.

Furthermore, Applicants respectfully submit that, even if Applicant's statement was somehow combined with Coutts, there would have been no reasonable expectation of success, based on the disclosures, to achieve the present invention. This is primarily because, given the statement made by Applicants, the teachings of Coutts make it extremely difficult for one of ordinary skill in the art to pinpoint a candidate compound with a reasonable chance of success, and therefore would not motivate one of ordinary skill in the art to tackle such tasks. This is especially true when considering the following reasons.

First of all, there is no consistency in examples given in Coutts as to which enantiomer has better pharmacological properties. This is because the optical rotation of

compounds in general has no direct correlation with their pharmacological activity. For example, the (-) enantiomer of thalidomide has been reported to be toxic (page 101, col. 1), whereas the (-) enantiomer of molindone is reported to be more useful than its (+) counterpart (page 106, col. 1). Furthermore, both enantiomers of some compounds are reported to be equally potent in their biological activity. For example, both enantiomers of 10-hydroxyamitriptyline have been shown to be "similar to one another in their abilities to inhibit NE and 5-HT uptake." *See Coutts* at page 116, col. 1. With these inconsistencies, all Coutts does is to provide a mere speculation that an enantiomer can be different, more harmful or beneficial. Therefore, one of ordinary skill in the art would not have any guidance from Coutts in picking out potential candidate that one enantiomer of which would show better pharmacological properties than the other.

Secondly, as Coutts itself discloses, there are numerous drugs which are administered as a racemic mixture. *See Coutts* at page 102, col. 1 ("In 1980, it was estimated that at least 398 drugs prescribed in the United States were racemic mixtures"). This would leave one of ordinary skill in the art with literally hundreds of potential candidates, from which he or she can attempt to separate out the optical enantiomers and test for the pharmacological properties of each enantiomer. Based on the inconsistencies disclosed in Coutts, one of ordinary skill in the art would not have expected a reasonable successful in any of the drugs.

Along the same line, Applicants respectfully submit that combining the disclosure in Applicants' specification that racemic bupropion is used for smoking cessation, with Coutts is purely based on impermissible hindsight. *See In re Sernaker*, 702 F.2d 989, 994 (Fed. Cir. 1983); *In re Rinehart*, 531 F.2d 1048 (CCPA 1976); *In re Imperato*, 486 F.2d 585 (CCPA 1973); *In re Adams*, 356 F.2d 998 (CCPA 1966). Consequently, it is legally improper to select from the prior art the separate components of the inventor's combination, using the blueprint supplied by the inventor. *C.R. Bard Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1352 (Fed. Cir. 1998) citing *Fromson v. Advance Offset Plate, Inc.*, 755 F.2d 1549, 1556 (Fed. Cir. 1985) (holding the prior art must suggest to one of ordinary skill in the art the desirability of the claimed combination).

Here, racemic bupropion's known use as a drug that treats smoking addiction does nothing to motivate one of ordinary skill in the art to proceed with separating out each enantiomer of bupropion, considering the fact that bupropion is merely one of hundreds of compounds which were commercially available at the time of the invention. In other words, absent a specific teaching in the prior art that bupropion is a better candidate than other known racemic drugs for being a drug that one enantiomer of which is pharmaceutically more favorable than the other, selecting bupropion is as random as selecting, for example, deprenyl.

For the foregoing reasons, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) should be withdrawn.

CONCLUSION

Applicants respectfully submit that the pending claims 16, 18-29, 43, 45-55, and 79-80 are in condition for allowance. Should the Examiner disagree, a personal or telephonic interview is respectfully requested to resolve any remaining issues in this application.

No fee is believed to be due for the submission of this response, except the fee for the Petition for Extension of Time Submitted herein. Should any additional fee be required, however, please charge such fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

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Enclosures